Bronchiectasis-COPD Overlap Syndrome (BCOS) among the Nepalese Patients: Emerging disease from a developing country

Achyut Bhakta Acharya[1], Narendra Bhatta[1], Deebya Raj Mishra[1], Prahlad Karki[2], Mukesh Kumar Gupta[3], Madhab Lamsal[4], Basuda Khanal[5]

[1] *Department of Pulmonary, Critical Care & Sleep Medicine, BP Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal;*
[2] *Department of Cardiology, B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal;*
[3] *Department of Radiodiagnosis, B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal;*
[4] *Department of Biochemistry, B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal;*
[5] *Department of Microbiology, B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal*

ABSTRACT

Background and objective: There is no clearly specified diagnostic criteria to identify BCOS in Nepalese context. So this first, observational cross-sectional study was conducted to determine the current situation, main clinical practices, and features of BCOS in Nepalese patients, exploring its clinical trajectory and severity.

Methods: This is a hospital based descriptive cross-sectional study conducted, where patients presenting with respiratory symptoms complex were subsequently enrolled by purposive sampling. Descriptive Statistics was calculated using Absolute and Relative Frequencies for categorical variables and mean and standard deviation for numerical ones. P-value of <0.05 was considered significant.

Results: Out of 236 patients of Respiratory Symptoms Complex, prevalence of BCOS was 22.03%. 57.7% were males with mean age of 67.8 years. Among BCOS cohorts, 92.3% were smokers and 73 % had significant exposure to indoor air pollution. 63.5% of the patients had past history of tuberculosis and cardio-metabolic co-morbidities were seen in 34.6% of the patients. The most frequent symptoms were cough and shortness of breath and the commonest sign was bilateral basal coarse crackles. Frequent exacerbations were present in 25% of the patients and PFT revealed obstructive pattern in 71% of the BCOS patients with a mean FACED score of 3.94±1.62.

Conclusion: Among the patients presenting with Respiratory symptom complex in Nepal, BCOS is common and is more prevalent in elderly male, having a high co-morbidities, usually following a course of slowly progressive breathlessness, with higher incidence of exacerbation and poorer functional outcome.

Keywords: BCOS, Bronchiectasis, COPD, FACED Score, Overlap Syndrome

INTRODUCTION

Bronchiectasis-COPD Overlap Syndrome (BCOS) is a discrete clinical entity meeting the structural diagnostic criteria of Bronchiectasis and Physiological criteria for the diagnosis of COPD.[1] There exists an unmet need on the data available regarding management of patients with Bronchiectasis-COPD Overlap as the patients are typically excluded from therapy trials for Bronchiectasis or COPD and thus, the understanding and necessity to include Bronchiectasis-COPD Overlap Syndrome seems important.

BCOS has not been studied in Nepal. So we aimed to study the prevalence of Bronchiectasis Chronic Obstructive Pulmonary Disease Overlap Syndrome (BCOS) among the patients presenting with Respiratory Symptom Complex in Nepal, exploring its clinical trajectory and impact on disease severity.

Corresponding author:
Achyut Bhakta Acharya,
Department of Pulmonary, Critical Care and Sleep Medicine,
B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal.
Email: achyutbhakta@gmail.com

METHODS:

This was a hospital based descriptive cross sectional study. For the purpose of this study, Respiratory Symptom Complex (RSC) was defined as respiratory symptoms like cough with or without expectoration, dyspnea, chest pain, and/or hemoptysis of 3 or more weeks duration. Bronchiectasis - COPD Overlap Syndrome (BCOS) was defined as a discrete clinical entity among the patients presenting with Respiratory Symptom Complex meeting the structural criteria for the diagnosis of bronchiectasis i.e. the presence of "Bronchiectatic" airway wall changes as evident on chest CT and physiological criteria for the diagnosis of COPD as defined by the spirometry values as defined by GOLD.[2] Only patients who demonstrated both the features of bronchiectasis and COPD were diagnosed as BCOS.

Figure 1 shows the Trial profile of the study.

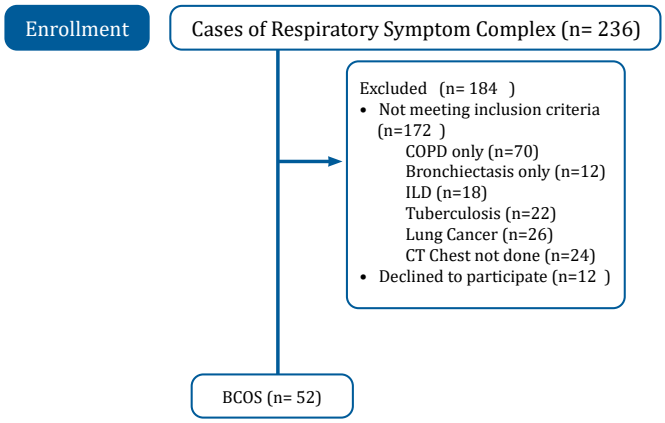

Figure 1 : Trial profile of the study

For the purpose of the study, the BRONCH-UK Consortium consensus statement[1] was utilized to provide descriptive definition of Bronchiectasis - COPD Overlap Syndrome (BCOS).

The FACED (FEV1, Age, Colonization, Extension of Bronchiectasis and Dyspnea)[3] Score was used as surrogate for ascertaining the clinical Severity of BCOS. By this score, BCOS was classified into 3 severity classes: Mild BCOS (Overall score 0-2 points), Moderate BCOS (Overall score 3-4 points) and Severe BCOS (Overall score 5-7 points). All patients had Pulmonary Function Test including measurement of Forced Vital Capacity (FVC) and FEV1 with recording the best result from three measurements, the values of which were within 5% of each other.

Patients were enrolled after signing the written consent. Clinical care and treatment was as per the standard clinical practice followed in the institute. Ethical clearance to conduct the study was obtained from the Institutional Ethical Review Board (IRC/1529/01). Patients were recruited from the inpatients and OPD following purposive sampling method, from March, 2020 to February 2021. A detailed history, socio-demographic data and physical examination for every patient were performed and information was recorded in structured proforma. Every patient was followed from admission to discharge to evaluate outcomes.

For Statistical Analysis, Descriptive Statistics was calculated using Absolute and Relative Frequencies, and for categorical variables, mean (Median) and Standard Deviation (Interquartile Range) for numerical ones. Fisher Exact Test was used to assess differences in categorical data. All Tests was two-tailed; a p-value of <0.05 was considered significant. Statistical Analysis was performed using SPSS version 22.0

RESULTS:

Among 236 patients presenting with Respiratory Symptoms Complex at our study center, prevalence of BCOS was 22.03%. The baseline characteristics of the patients of BCOS are displayed in table 1.

Table 1: Baseline characteristics of the patients of BCOS (n=52)

Characteristics	N (%)
Age (mean ± SD) (Years)	67.8 ± 9.5
Gender	Male 30(57.7)
Residential Address	
Plain Region	38 (73.1)
Hill Region	14 (26.9)
Occupation	
Agriculture	33 (63.5)
Business	6 (11.5)
Household Work	9 (17.3)
Industries	4 (7.6)
Tobacco Smoking	48 (92.3), Yes
Former Smoker	42 (80.8)
Current Smoker	6 (11.5)
Never Smoker	4 (7.7)

92.3% of patients with BCOS were tobacco smokers, majority (82%) smoking more than 10 pack years. Most (48%) had started to smoke tobacco at the age of 15 years.

Nearly 73% of our patients with BCOS had significant history of exposure to indoor air pollution. Nearly 63.5% of the patients with BCOS had past history of pulmonary tuberculosis. Cardiovascular comorbidities was seen in 13(25%) of the patients, whereas Metabolic comorbidities were seen in 5 (9.6%) of the patients.

All of our patients with BCOS presented with persistent cough and 84.6% with profuse purulent sputum, while shortness of breath was present in 96.2% of patients. Fever was reported by 50% of our patients with BCOS. Around 25% of our patients had multiple course of antibiotics during the study period. Around 25% of our patients with BCOS had swelling of bilateral lower limb. Around 17.3% of our patients with BCOS had chest pain.

In our study, bilateral basal coarse crackles were heard in 64% of patients with BCOS. Wheezing was less common, present in 54% of the study population. 23.1% of the patients had bilateral pedal edema. Surprisingly digital clubbing, was found only in 3.8% of BCOS patients and majority (80.8%) of the patients had normal BMI. 71% of our patients with BCOS showed obstructive pattern of pulmonary function on spirometry. 44% patients of BCOS had respiratory failure either during their presentation or during the hospital stay, requiring care in the ICU. 83% of our patients with BCOS had moderate to severe FACED score, with mean FACED score of 3.94±1.62.

Table 2 shows the severity among the BCOS cohorts as per the FACED score.

Table 2 Severity among the BCOS cohorts as per the FACED score

Severity as per FACED Score	BCOS patients(n)	Percentage (%)
Mild	9	17.3
Moderate	28	53.8
Severe	15	28.9

Radiological features of Bronchiectasis in Patients with BCOS is presented in the Table 3.

Table 3: Radiological features of Bronchiectasis in Patients with BCOS

Type of Bronchiectasis	Number of Patients	Percentage (%)
Cystic	51	96.1%
Saccular	1	3.9%
Location of Bronchiectasis		
Lower Lobe	33	63.5%
Upper Lobe	10	19.2%
Bilaterality		
Bilateral	38	73.1%
Unilateral	14	26.9%
Thickening of Bronchial wall		
Mild	23	44.2%
Moderate	28	53.8%
Severe	1	1.9%

DISCUSSION:

Among the patients presenting with Respiratory Symptom Complex, the prevalence of BCOS was 22% in our study. The reported prevalence of BCOS, varies widely, depending on the criteria used and the population studied[1,4-6] ranging from 19.9%[7] in one study to 54.3%[8] in the other.

In our study, most were male with the mean age of 67.8 years and our findings are similar to those of previous studies.[9,10]

Majority of our patients with BCOS had history of Pulmonary Tuberculosis before being diagnosed as BCOS which might have been the cause of Bronchiectasis itself. The strongest associations between Tuberculosis and Bronchiectasis have been observed in countries with a high incidence of tuberculosis.[11]

Smoking is the conventional risk factor for COPD and a known agent for causing exacerbation in COPD as well as bronchiectasis.[12] So, the finding of high prevalence of tobacco smoking among our patients with BCOS in our study might points towards some role in either causing BCOS or may be the agent for exacerbation.

Our patients with BCOS, revealed significant co-morbidities, in around 34.6%(18 out of 52) of patients which might be due to the common denominator of systemic inflammation and perhaps may be one of the most important modifying risk factors for severity in BCOS.

Chronic productive cough with shortness of breath were the main presenting symptoms in our patients of BCOS whereas bilateral basal coarse crackles was the main sign. Characteristically in these patients, wheezing and clubbing were less common, though their presence indicated severe form of disease. Most of our patients had normal BMI. Our finding is in contrast to the study done previously by Lei Shi, Feng-Xian Wei in 2020[13] and Ernesto Crisafulli et al[14], where their subjects had low BMI. In comparison to COPD and Bronchiectasis patients, who have low BMI, our patients were relatively preserved, exact cause couldn't be explained.

Acute worsening and respiratory failure leading to emergency visit and hospitalization is common among BCOS. Around 25% of our patients had taken multiple course of antibiotics during the study period. This could be explained by the known fact that these patients have increased susceptibility to pulmonary infection due to the intense inflammatory process itself and due to the frequent use of steroid medication during the exacerbation. And also it is a known fact that smokers are more prone for recurrent infection due to the impaired ciliary function of the tracheobronchial tree. Majority of our patients were enrolled from the inpatient services which also reflects that these people have recurrent hospital admission which has been reported recently in a study done in 2020.[13]

We employed the FACED score to identify severity and prognostication in patients with BCOS in our study. Majority of our patients had moderate to severe FACED score which implies contribution of the Bronchiectasis component to be in severe form. At present, there are no scales that can be used to assess the severity and the prognosis of the BCOS. In this context, the FACED score can have point of care utility in providing a quick assessment of the initial severity, severe exacerbation requiring hospitalization in a multidimensional and heterogeneity disease like BCOS.

Pattern of Pulmonary Functions Test in Patients with BCOS was more of the Obstructive Type (71%, 37 out of 52). Finding of Obstructive pattern in spirometry reveals more severe form of disease and a higher frequency of hospital admissions in patients of BCOS in our study. The degree of impaired pulmonary function in patients with BCOS depends also on the associated clinical conditions, in particular tobacco smoking, which accelerates the obstructive damage and reduces the pulmonary function.

It was interesting to note that most of our patients with BCOS had bilateral Bronchiectasis which was mostly cystic type mostly in the lower lobe and with moderate amount of Bronchial Wall Thickening. It was striking to note that these patients with BCOS had unilateral Bronchiectasis in only 26.9% of the cases which could likely be due to Tuberculosis, which is highly prevalent in our country.

In our study, isolation of potential pathogenic microorganisms in sputum of patients with BCOS was very low. Our hospital being a tertiary care center, we receive mostly referred case or primarily managed in another hospital, so the number of isolated organisms were low. The one where organisms were isolated, these patients had the most severe disease, showing the worst radiological and highest inflammatory patterns with lowest functional status and highest number of exacerbations and hospitalizations, which is in concordance with the study done by Qihong Yu et al in 2019.[15]

LIMITATION

Limitation of the study is the possibility of selection bias, which could not be ruled out on account of the study design. This could have resulted in misclassification of patients in the analysis. It is also important to note that our study focused on the prevalence and burden of BCOS in a Hospital-based population.

To the best of our knowledge this is the first study from Nepal. Information from this study provides new direction towards our understanding, challenges the earlier approach of a simplistic diagnostic dichotomy between Bronchiectasis and COPD, and provides evidence that tobacco smoking, toxic exposure to indoor air pollution and past pulmonary tuberculosis may cause Bronchiectasis -dominant, COPD-dominant, or BCOS pathology, with differing implications for treatment, complications, and prognosis.

CONCLUSION

Thus, we conclude that substantial number of patients presenting with Respiratory Symptom Complexes in Nepal, have BCOS and points that BCOS is a relatively common, yet unrecognized and undiagnosed disease that can be linked to the epidemic of tobacco smoking, high exposure to indoor air pollution, high burden of post Tubercular sequelae and workforce exposed to agrarian/farming and industrial occupation in Nepal and have distinct natural history with severe symptoms, high occurrence of co-morbidities, with high incidence of exacerbation and poorer functional outcome

ACKNOWLEDGEMENTS:

I like to thank all the patients involved in this study.

CONFLICT OF INTEREST:

None

REFERENCES

1. Hurst JR, Elborn JS, Soyza A De. COPD–bronchiectasis overlap syndrome. Eur Respir J [Internet]. 2015 Feb 1;45(2):310 LP – 313. Available from: http://erj.ersjournals.com/content/45/2/310.abstract
2. Halpin DMG, Criner GJ, Papi A, Singh D, Anzueto A, Martinez FJ, et al. Global Initiative for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. Am J Respir Crit Care Med. 2021 Jan 1;203(1):24–36.

3. Martínez-García MÁ, De Gracia J, Relat MV, Girón R-M, Carro LM, de la Rosa Carrillo D, et al. Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score. Eur Respir J. 2014;43(5):1357–67.
4. Chalmers JD. Bronchiectasis and COPD Overlap: A Case of Mistaken Identity? Chest [Internet]. 2017;151(6):1204–6. Available from: http://dx.doi.org/10.1016/j.chest.2016.12.027
5. Dou S, Zheng C, Cui L, Xie M, Wang W, Tian H, et al. High prevalence of bronchiectasis in emphysema-predominant COPD patients. Int J Chron Obstruct Pulmon Dis [Internet]. 2018 Jun 27;13:2041–7. Available from: https://pubmed.ncbi.nlm.nih.gov/29988718
6. Arram EO, Elrakhawy MM. Bronchiectasis in COPD patients. Egypt J Chest Dis Tuberc [Internet]. 2012;61(4):307–12. Available from: http://dx.doi.org/10.1016/j.ejcdt.2012.07.001
7. Tan WC, Hague CJ, Leipsic J, Bourbeau J, Zheng L, Li PZ, et al. Findings on Thoracic Computed Tomography Scans and Respiratory Outcomes in Persons with and without Chronic Obstructive Pulmonary Disease: A Population-Based Cohort Study. PLoS One [Internet]. 2016 Nov 18;11(11):e0166745–e0166745. Available from: https://pubmed.ncbi.nlm.nih.gov/27861566
8. Ni Y, Shi G, Yu Y, Hao J, Chen T, Song H. Clinical characteristics of patients with chronic obstructive pulmonary disease with comorbid bronchiectasis: A systemic review and meta-analysis. Int J COPD. 2015;10(1):1465–75.
9. Gatheral T, Kumar N, Sansom B, Lai D, Nair A, Vlahos I, et al. COPD-related Bronchiectasis; Independent Impact on Disease Course and Outcomes. COPD J Chronic Obstr Pulm Dis [Internet]. 2014 Dec 1;11(6):605–14. Available from: https://doi.org/10.3109/15412555.2014.922174
10. Jin J, Yu W, Li S, Lu L, Liu X, Sun Y. Factors associated with bronchiectasis in patients with moderate-severe chronic obstructive pulmonary disease. 2016 [cited 2020 Dec 27]; Available from: http://dx.doi.org/10.1097/MD.0000000000004219
11. Byrne AL, Marais BJ, Mitnick CD, Lecca L, Marks GB. Tuberculosis and chronic respiratory disease: a systematic review. Int J Infect Dis [Internet]. 2015;32:138–46. Available from: https://www.sciencedirect.com/science/article/pii/S1201971214017330
12. Olloquequi J, Silva R. Biomass smoke as a risk factor for chronic obstructive pulmonary disease: effects on innate immunity.
13. Shi L, Wei F, Ma T, Zhou W, Li M, Wan Y. Impact of Radiographic Bronchiectasis in COPD. Respir Care. 2020;
14. Crisafulli E, Guerrero M, Ielpo A, Ceccato A, Huerta A, Gabarrús A, et al. Impact of bronchiectasis on outcomes of hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease: A propensity matched analysis. Sci Rep [Internet]. 2018;8(1):9236. Available from: https://doi.org/10.1038/s41598-018-27680-y
15. Yu Q, Peng H, Li B, Qian H, Zhang H. Characteristics and related factors of bronchiectasis in chronic obstructive pulmonary disease. Medicine (Baltimore). 2019;98(47).